Abstract OP20

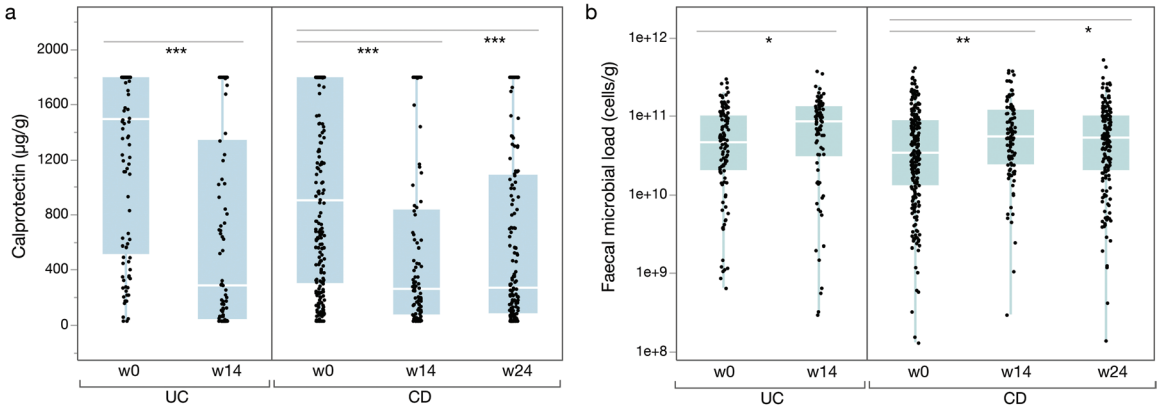

Figure 3. *Longitudinal measurements of FCal (µg/g faeces) and microbial loads (microbial cells/gram faeces) during the treatment period for the UC and CD cohorts. Kruskal- Wallis with posthoc Dunn test p<0.05 [*], p<0.01 [**], p<0.001 [***].*

Conclusion: The prevalence of the inflammatory Bact2 enterotype was 5- to 10-fold higher in CD and UC patients as compared with controls. Although initiation of biological therapies leads to a decrease in inflammation levels as witnessed by faecal calprotectin and increase in microbial richness, a shift in enterotypes did not occur.

OP21

Positivity thresholds of total infliximab and adalimumab anti-drug antibody assay: The prevalence of clearing and transient anti-drug antibodies in a national therapeutic drug monitoring service

R. Nice[1], N. Chanchlani*[2], H. Green[2], C. Bewshea[2], N. Kennedy[2], T. Ahmad[2], J. Goodhand[2], T. McDonald[1], M. Perry[1]
[1]*Department of Blood Sciences, Royal Devon and Exeter Hospital, NHS Foundation Trust, Exeter, UK,* [2]*Exeter IBD Pharmacogenetics, University of Exeter., Exeter, UK*

Background: Anti-drug antibodies can affect biopharmaceutical pharmacokinetics by increasing or decreasing drug clearance. Drug-tolerant (total), unlike drug-sensitive (free), antibody assays permit antibodies to be measured in the presence of a drug. We sought to confirm the positivity threshold of our total anti-tumour necrosis factor (TNF) antibody ELISA assays in a sample of healthy volunteers and to use this threshold to report the prevalence of clearing and transient antibodies in patients treated with infliximab and adalimumab.

Methods: Serum was obtained from a random sample of 498 anti-TNF-naïve healthy adults recruited to the Exeter Ten Thousand study and tested for total anti-drug antibodies to infliximab and adalimumab. Using recommendations for confirmatory anti-drug antibody validation, we used bootstrapping to calculate the 80% one-sided lower confidence interval [CI] of the 99th centile to define assay thresholds. We used paired drug and anti-drug antibody levels derived from our national therapeutic drug monitoring service to report the distribution of clearing (antibody positive, drug negative) vs. non-clearing (antibody positive, drug positive) antibodies. In patients with at least two test results, antibodies were classified as transient (single positive test with subsequent negative test) or persistent (at least two positive tests).

Results: The 80% one-sided lower CI of the 99th centile titre for total anti-drug antibody to infliximab and adalimumab were 8.7 AU/ml and 5.9 AU/ml, respectively. Using the manufacturer's recommended threshold of 10 AU/ml for both total anti-TNF antibody assays, in healthy individuals, the prevalence of positive antibodies to infliximab and adalimumab was 1% (5/498) and 0.2% (1/498), respectively. Using the manufacturer's threshold, at the time of last testing, of 7447 and 4054 patients treated with infliximab and adalimumab; 20.9% (*n* = 1,554) and 8.0% (*n* = 326) had clearing antibodies and 26.5% (*n* = 1973) and 12.1% (*n* = 490) had non-clearing antibodies, respectively (Figure 1). Using our newly defined threshold in the same cohorts; 21.1% (*n* = 1573) and 8.4% (*n* = 339) had clearing antibodies and 28.0% (*n* = 2083) and 20.0% (*n* = 812) had non-clearing antibodies, to infliximab and adalimumab, respectively. Amongst patients with at least two tests, most developed persistent antibodies (Figure 2). Irrespective of anti-TNF drug, or threshold used, less than 10% patients developed transient antibodies.

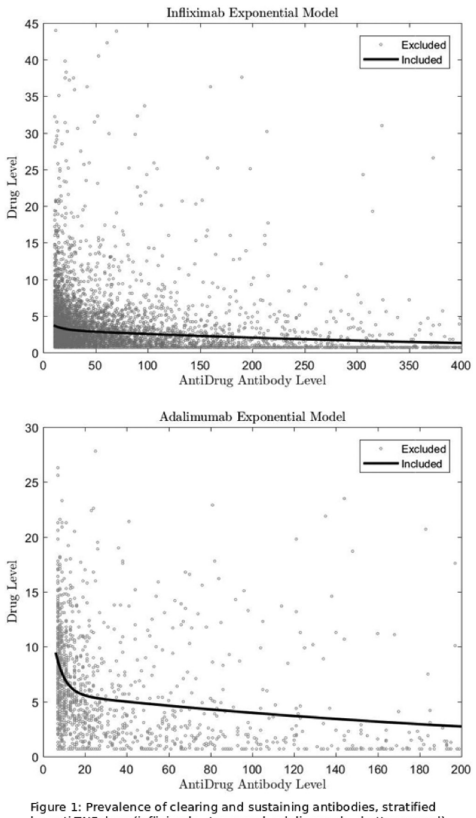

Figure 1: Prevalence of clearing and sustaining antibodies, stratified by anti-TNF drug (infliximab – top panel, adalimumab – bottom panel)

Abstract OP21

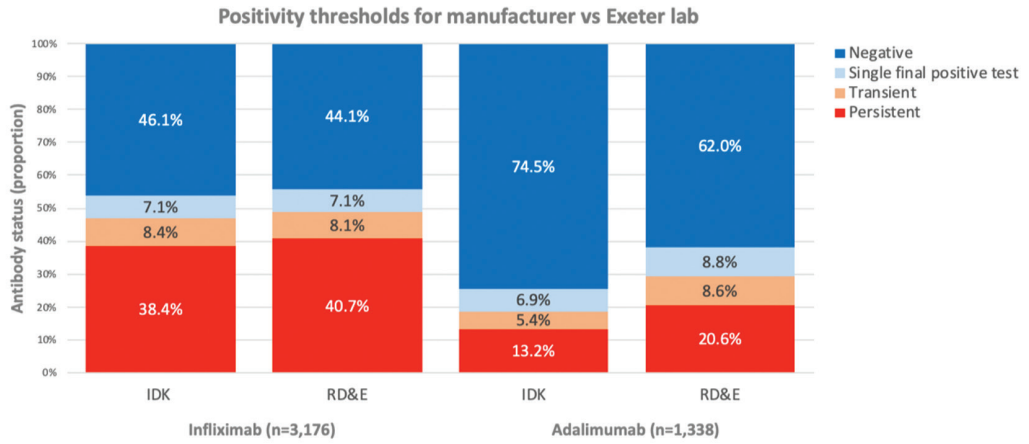

Figure 2: Antibody status, stratified by manufacturer (IDK) or Exeter lab (RD&E) positivity threshold, by anti-TNF drug

Conclusion: We report lower positivity thresholds for the IDKmonitor® total anti-TNF antibody ELISA assays than the manufacturer, in particular, for adalimumab. Transient antibody formation is uncommon: most patients develop persistent anti-drug antibodies that lead to drug clearance.

OP22

Crohn's disease exclusion diet reduces bacterial dysbiosis towards healthy controls in paediatric Crohn's disease

J. Van Limbergen*[1], K. Dunn[2], E. Wine[3], R. Sigall Boneh[4], J. Bielawski[2], A. Levine[4]

[1]*Division of Pediatric Gastroenterology and Nutrition, Amsterdam UMC - Location AMC, Amsterdam, The Netherlands,* [2]*Department of Biology, Dalhousie University, Halifax, Canada,* [3]*Department of Paediatric Gastroenterology and Nutrition, University of Alberta, Edmonton, Canada,* [4]*Wolfson Medical Centre, Paediatric Gastroenterology & Nutrition, Holon, Israel*

Background: Dietary therapy with the Crohn's disease Exclusion Diet (CDED) or Exclusive Enteral Nutrition (EEN) induces remission, reduces inflammation and is associated with compositional changes in the microbiome. We performed metagenome analysis to elucidate whether diet induces remission via correction of dysbiosis and/or community structure.

Methods: Whole metagenome and 16S rDNA sequences were obtained in 178 samples from 70 participants at 3 time points (baseline, week 6, week 12) from the two study groups (CDED+PEN/EEN). For metagenome analysis, we divided the groups further into samples of patients achieving ITT-remission at week 6 (CDED+PEN: 31/38 and EEN: 23/32) and those who did not.

Results: Dietary therapy decreased the relative abundance of genera from Proteobacteria towards healthy controls. CDED+PEN remission is associated with a significant increase ($p < .05$) in *Clostridiales*, and a significant decrease ($p < .05$) in Proteobacteria (particularly Γproteobacteria). Microbiome comparison of all baseline CD samples with healthy controls showed significant ($p < .05$) increases in Proteobacteria in an active CD at baseline. Healthy controls had increased Firmicutes species notably *Roseburia*, *Oscillibacter* and *Anaerostipes*, as well as increased *Bacteroides* and Ascomycota (driven by *Saccharomyces*). Proteobacteria decreased when diet-induced remission was achieved (with either CDED+PEN or EEN) at week 6: relative abundance of Proteobacteria (including A- and Γproteobacteria (e.g. *Escherichia*, *Klebsiella* and *Citrobacter*) were significantly lower compared with baseline but were still more abundant in CD patients,